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(FILE 'HOME' ENTERED AT 17:02:07 ON 26 FEB 2004) FILE 'CAPLUS' ENTERED AT 17:02:15 ON 26 FEB 2004 0 S SOFTWARE AND ((3(2W)D) OR (THREE(2W)DIMENSIONAL) (2W) IMAGE) L164 S ((3(2W)D) OR (THREE(2W)DIMENSIONAL) (2W) IMAGE) AND MODELLI L23 S L2 AND REVIEW/DT L361 S L2 NOT L3 L4L55 S L4 AND PATENT/DT L6 56 S L4 NOT L5 L7 23 S L6 AND PY<2001 FILE 'WPIDS' ENTERED AT 17:07:56 ON 26 FEB 2004 FILE 'USPATFULL' ENTERED AT 17:08:08 ON 26 FEB 2004 20168 S 702/?/NCL $\Gamma8$ 1435 S L8 AND ((3(2W)D) OR (THREE(2W)DIMENSIONAL) (2W) IMAGE) L980 S L9 AND MODELLING L1052 S L10 AND (CHEM? OR BIOL?) L1132 S L10 AND LIGAND L12 280 S L8 AND CRYSTAL AND ((3(2W)D) OR (THREE(2W)DIMENSION?) AND L13

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(FILE 'HOME' ENTERED AT 14:05:01 ON 26 FEB 2004)

FILE 'CAPLUS' ENTERED AT 14:05:14 ON 26 FEB 2004 L1 41 S ULTRASPIRACLE PROTEIN

=> d bib, abs 3-6, 10-13, 17, 25, 27

L1 ANSWER 3 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

Full Text

AN 2003:310593 CAPLUS

DN 139:80985

TI Purification of Drosophila melanogaster **Ultraspiracle protein** and analysis of its A/B region-dependent dimerization behavior in vitro

AU Rymarczyk, Grzegorz; Grad, Iwona; Rusek, Agnieszka; Oswiecimska-Rusin, Kamila; Niedziela-Majka, Anita; Kochman, Marian; Ozyhar, Andrzej

CS Institute of Organic Chemistry, Biochemistry and Biotechnology, Division of Biochemistry, Wroclaw University of Technology, Wroclaw, 50-370, Pol.

SO Biological Chemistry (2003), 384(1), 59-69 CODEN: BICHF3; ISSN: 1431-6730

PB Walter de Gruyter GmbH & Co. KG

DT Journal

LA English

Two members of the nuclear receptor superfamily, EcR (ecdysteroid receptor AΒ protein) and Usp (Ultraspiracle), heterodimerize to form a functional receptor for the steroid hormone 20-hydroxyecdysone and thus enable it to coordinate morphogenetic events during insect metamorphosis. N-terminally His-tagged Usp was overexpressed in E. coli cells as a non-truncated protein and purified to homogeneity in two chromatog. steps. It was demonstrated that the recombinant receptor specifically binds the ecdysone response element of the hsp27 gene promoter (hsp27Ecker). Moreover, a highly synergistically formed heterodimeric complex with the DNA-binding domain of EcR was obsd. on hsp27EcRE, but not on the native Usp response element from the chorion s15 gene promoter. Recombinant Usp forms homodimers and homotetramers in the absence of DNA, as judged from gel filtration and chem. crosslinking expts. Truncation of its N-terminal A/B region changes mol. characteristics of Usp, considerably weakening its oligomerization potential under the same exptl. conditions. This contrasts with the results obtained previously for the similarly truncated RXR - a vertebrate homolog of Usp.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 4 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

Full Text

AN 2003:243738 CAPLUS

DN 139:347619

TI Using nondenaturing mass spectrometry to detect fortuitous ligands in orphan nuclear receptors

AU Potier, Noelle; Billas, Isabelle M. L.; Steinmetz, Anke; Schaeffer, Christine; Van Dorsselaer, Alain; Moras, Dino; Renaud, Jean-Paul

CS Laboratoire de Spectrometrie de Masse Bio-Organique, Ecole Europeenne de Chimie, Polymeres et Materiaux, CNRS UMR7509, Strasbourg, 67087, Fr.

SO Protein Science (2003), 12(4), 725-733 CODEN: PRCIEI; ISSN: 0961-8368

PB Cold Spring Harbor Laboratory Press

DT Journal

LA English

- Nondenaturing electrospray mass spectrometry (ESI-MS) has been used to AΒ reveal the presence of potential ligands in the ligand-binding domain (LBD) of orphan nuclear receptors. This new approach, based on supramol. mass spectrometry, allowed the detection and identification of fortuitous ligands for the retinoic acid-related orphan receptor β (ROR β) and the ultraspiracle protein (USP). These fortuitous ligands were specifically captured from the host cell with the proper stoichiometry. After org. extn., these mols. have been characterized by classic anal. methods and identified as stearic acid for ROReta and a phosphatidylethanolamine (PE) for USP, as confirmed by crystallog. These mols. act as "fillers" and may not be the physiol. ligands, but they prove to be essential to stabilize the active conformation of the LBD, enabling its crystn. The resulting crystal structures provide a detailed picture of the ligand-binding pocket, allowing the design of highly specific synthetic ligands that can be used to characterize the function of orphan nuclear receptors. An addnl. advantage of this new method is that it is not based on a functional test and that it can detect low-affinity ligands.
- RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L1 ANSWER 5 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

Full Text felo

AN 2003:230891 CAPLUS

DN 139:18590

- TI Effect of ecdysone agonists on vitellogenesis and the expression of EcR and USP in codling moth (Cydia pomonella)
- AU Sun, Xiaoping; Song, Qisheng; Barrett, Bruce
- CS Department of Entomology, University of Missouri, Columbia, MO, 65211, USA
- SO Archives of Insect Biochemistry and Physiology (2003), 52(3), 115-129 CODEN: AIBPEA; ISSN: 0739-4462
- PB Wiley-Liss, Inc.
- DT Journal
- LA English
- AB The effects of tebufenozide and methoxyfenozide on vitellogenin (Vg) synthesis/release in the fat body, translocation in hemolymph, uptake by the ovary, and the expression of the ecdysone receptor (EcR) and its heterodimer partner, ultraspiracle protein (USP) in fat body, were investigated in Cydia pomonello. The results indicated that both ecdysone agonists significantly increased the Vg level in the adult hemolymph when the moths were exposed to agonist-treated surfaces. However, these agonists did not affect Vg release from the fat body nor Vg deposition in the first batch oocytes. Western blot anal. revealed that the expression of EcR and USP was significantly increased in tebufenozide— and methoxyfenozide—treated samples compared to the control, suggesting that ecdysone agonists regulated the Vg synthesis via the EcR and USP proteins complex.
- RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L1 ANSWER 6 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
- Text 2003:227261 CAPLUS
- DN 139:209479
- TI Structure-based analysis of the **ultraspiracle protein** and docking studies of putative ligands
- AU Sasorith, Souphatta; Billas, Isabelle M. L.; Iwema, Thomas; Moras, Dino; Wurtz, Jean-Marie
- CS Dep. Genomique Biologie Structurales, Inst. Genetique Biologie Moleculaire Cellulaire, Illkirch, 67404, Fr.

SO Journal of Insect Science (Tucson, AZ, United States) [online computer file] (2002), 2, No pp. given CODEN: JISTCY; ISSN: 1536-2442

URL: http://www.insectscience.org/2.25/Sasorith et.al. JIS 2 25 2002.pdf

- PB University of Arizona Library
- DTJournal; (online computer file)
- LΑ English
- The ultraspiracle protein (USP) is the insect ortholog of the AΒ mammalian retinoid X receptor (RXR). Fundamental questions concern the functional role of USP as the heterodimerization partner of insect nuclear receptors such as the ecdysone receptor. The crystallog. structures of the ligand binding domain of USPs of Heliothis virescens and Drosophila melanogaster solved recently show that helix 12 is locked in an antagonist conformation raising the question whether USPs could adopt an agonist conformation as obsd. in RXRa. In order to investigate this ° hypothesis, a homol. model for USP is proposed that allows a structural anal. of the agonist conformation of helix 12 based on the sequence comparison with RXR. For USP, one of the main issues concerns its function and in particular whether its activity is ligand independent or The x-ray structures strongly suggest that USP can bind ligands. Putative ligands have therefore been docked in the USP homol. model. Juvenile hormones and juvenile hormone analogs were chosen as target ligands for the docking study. The interaction between the ligand and the receptor are examd. in terms of the pocket shape as well as in terms of the chem. nature of the residues lining the ligand binding cavity.
- THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 10 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

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Text
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AN 2002:658234 CAPLUS

137:196680 DN

- Substitution variants of nuclear receptors and their use in a dual switch ΤI inducible system for regulation of gene expression
- IN Palli, Subba Reddy; Kumar, Mohan Basavaraju; Cress, Dean Ervin; Fujimoto, Ted Tsutomu
- Rohm and Haas Company, USA; Rheogene Inc. PΑ
- PCT Int. Appl., 148 pp. SO CODEN: PIXXD2
- DTPatent
- LΑ English

FAN.CNT 6

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APPLICATION NO.
     PATENT NO.
                        KIND
                              DATE
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                                               wo 2002-, ús5090
PΙ
        2002066612
                         A2
                              20020829
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                        А3
                              20031030
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              CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
              GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
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              TJ, TM
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     EP 1373470
                         A2
                              20040102
                                               EP 2002-742489
                                                                20020220
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI US 2001-269799P
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                              20010220
     US 2001-313925P
                         Ρ
                              20010821
     WO 2002-US5090
                              20020220
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MARPAT 137:196680 os

AΒ This invention relates to the field of biotechnol. or genetic engineering. A mechanism for the regulation of gene expression that allows tight control of a no. of genes is described. The transactivation and DNA-binding domains of transcription regulatory factors are sepd. by placing them on two different protein cassettes. The transactivation and DNA-binding domains of transcription regulatory factors are sepd. by placing them on two different fusion proteins. The chimeric genes encoding the fusion proteins encode a first protein that is a DNA-binding domain fused to a nuclear receptor and the second encoding a transactivation domain fused to a nuclear receptor polypeptide. Interaction of the first protein with the second protein effectively tethers the DNA-binding domain to the transactivation domain. Since the DNA-binding and transactivation domains reside on two different mols., the background activity in the absence of ligand is greatly reduced. Novel substitution mutant of nuclear receptors, specifically Group H nuclear receptors, that show improved ligand responsiveness that can be used to modulate gene expression in a host cell for applications such as gene therapy, large scale prodn. of proteins and antibodies, cell-based high throughput screening assays, functional genomics and regulation of traits in transgenic organisms. In particular, one gene expression cassette is inducibly regulated by a steroid ligand and the other gene expression cassette is inducibly regulated by a non-steroid ligand. Specific embodiments of the invention provide ecdysone receptor ligand-binding domains fused to the DNA-binding domains of GAL4 or LexA, and the ligand-binding domains of retinoid X receptor or ultraspiracle protein fused to the VP16 transactivation domain. A series of substitution mutants of insect ecdysteroid receptors were prepd. by std. PCR mutagenesis and tested for their responsiveness to ecdysteroid induction of reporter gene expression in the dual switch system. Variants that showed increased responsiveness to the ecdysteroids with decreased responsiveness to non-steroid ligands were identified. Variants showed increased responsiveness to both classes of effectors, or to nonsteroids but not ecdysteroids, were also identified.

ANSWER 11 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

Full

2002:276176 CAPLUS AN

DN 136:305140

ΤI Ecdysone receptor, retinoid X receptor and ultraspiracle protein based dual switch inducible gene expression modulation system

Dhadialla, Tarlochan Singh; Cress, Dean Ervin; Carlson, Glenn Richard; IN Hormann, Robert Eugene; Palli, Subba Reddy; Kudla, Arthur John; Herzig, Ronald Phillip, Jr.; Philip, Mohan

PΑ Rohm and Haas Company, USA

SO PCT Int. Appl., 79 pp. CODEN: PIXXD2

DT Patent

English LA

FAN.CNT 1																	
	PATENT	NO.		KI	ND	DATE			Α	PPLI	CATI	ON N	ο.	DATE			
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PI	WO 2002029075			A2		20020411		WO 2001-US30608					80	20010928			
	WO 2002029075			A3		20021031											
	WO 2002	0290	<u>75</u>	С	1	2002	1227										
	WO 2002029075			C2		20030220											
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
		co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
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             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                           US 2001-965697
                            20020815
                                                             20010927
    US 2002110861
                       Α1
                                           AU 2001-94916
     AU 2001094916
                            20020415
                       Α5
                                                             20010928
                                           EP 2001-975606
    EP 1334200
                       A2
                            20030813
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             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
                            20001003
PRAI US 2000-237446P
                      Ρ
     US 2001-965697
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    WO 2001-US30608
                       W
                            20010928
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The present invention relates to the field of biotechnol. or genetic AΒ engineering. More specifically, the present invention relates to a multiple inducible gene regulation system that functions within cells to simultaneously control the quant. expression of multiple genes. The transactivation and DNA-binding domains of transcription regulatory factors are sepd. by placing them on two different protein cassettes. improved gene expression system comprises two chimeric gene expression cassettes; the first encoding a DNA-binding domain fused to a nuclear receptor polypeptide and the second encoding a transactivation domain fused to a nuclear receptor polypeptide. Interaction of the first protein with the second protein effectively tethers the DNA-binding domain to the transactivation domain. Since the DNA-binding and transactivation domains reside on two different mols., the background activity in the absence of ligand is greatly reduced. In particular, one gene expression cassette is inducibly regulated by a steroid ligand and the other gene expression cassette is inducibly regulated by a non-steroid ligand. Specific embodiments of the invention provide ecdysone receptor ligand-binding domains fused to the DNA-binding domains of GAL4 or LexA, and the ligand-binding domains of retinoid X receptor or ultraspiracle protein fused to the VP16 transactivation domain.

ANSWER 12 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

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Peterences
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2002:157150 CAPLUS AN

136:197331 DN

Identification of the Heliothis virescens homolog of the ultraspiracle TТ protein by sequence homology and the development of novel insecticides

IN Zitzmann, Werner; Franken, Eva-Maria; Janssen, Martina; Schulte, Thomas

PΑ Bayer A.-G, Germany

Eur. Pat. Appl., 13 pp. SO CODEN: EPXXDW

DТ Patent

LΑ German

FAN.CNT 1

	PAT	CENT	NO.		KI	ND	DATE			A	PLIC	CATI	ON NO	ο.	DATE			
PI	EP	1183	2212		A.	2	2002	0227		E	200	01-1	1661	<u>6</u>	2001	0712		
	EP	118	<u> 2212</u>		A.	3	2002	0306										
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
			ΙE,	SI,	LT,	LV,	FI,	RO										
	DE	100	<u> 36469</u>		A	1	2002	0228		DE	200	00-1	00364	<u> 169</u>	2000	0725		
	JP	200	23454	84	A :	2	2002	1203		JI	200	01-2	1808	<u>l</u>	2001	0718		
	US	200	20375	<u>56</u>	A.	1	2002	0328		<u>U</u> :	200	01-9	09672	2	2001	0720		
PRAT	DE.	200	0 - 100	3646	φ Δ		2000	0725										

The Heliothis virescens homolog of the juvenile hormone receptor ultraspiracle is identified. The protein may be useful as a target for novel insecticides.

ANSWER 13 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

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AN
     2002:87199
                 CAPLUS
DN
     136:130549
     The three-dimensional structure of the ligand binding domain of
TI
     ultraspiracle protein (USP) and its use in the design of ligands for
     the domain
    Franken, Eva-Maria; Janssen, Martina; Schindler, Michael; Tietjen, Klaus;
     Moras, Dino; Wurtz, Jean-Marie; Rochel-Guibertau, Natacha;
     Billas-Massobrio, Isabelle
PΑ
     Bayer A.-G., Germany
SO
     Eur. Pat. Appl., 87 pp.
     CODEN: EPXXDW
DT
     Patent
     German
LA
FAN.CNT 1
                                            APPLICATION NO.
                                                              DATE
     PATENT NO.
                      KIND
PI
     EP 1176152
                       A2
                             20020130
                                            EP 2001-116617
                                                              20010712
     EP 1176152
                       Α3
                             20021211
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
                                                                             this of 4
                                            DE 2000-10036461 20000725
     DE 10036461
                       Α1
                             20020207
     US 2003027984
                                            us 2001-909556
                             20030206
                                                              20010720
                       Α1
     JP 2002363198
                             20021218
                       A2
                                                              20010725
PRAI DE 2000-10036461 A
                             20000725
     The three-dimensional structure of the ligand-binding domain of the
     ultraspiracle protein of Heliothis virescens is detd. by X-ray
     diffractometry. Factors affecting the response of the receptor to ligand
     binding and its transition between antagonistic and agonistic conformation
     are identified.
L1
     ANSWER 17 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
            Text
          AN
     2001:278087 CAPLUS
DN
     134:349657
     Crystal structure of the ligand-binding domain of the ultraspiracle
     protein USP, the Ortholog of retinoid X receptors in insects
     Billas, Isabella M. L.; Moulinier, Luc; Rochel, Natacha Moras, Dino
Genomics and Structural Biol. Lab., Inst. Genetique Biol. Mol. Cellulaire
ΑU
CS
     CNRS/INSERM, Univ. Louis Pasteur, Illkirch, 67404, Fr.
     Journal of Biological Chemistry (2001), 276(10), 7465-7474
SO
     CODEN: JBCHA3; ISSN: 0021-9258
PΒ
     American Society for Biochemistry and Molecular Biology
DT
     Journal
LΑ
     English
AB
     The major postembryonic developmental events happening in insect life,
     including molting and metamorphosis, are regulated and coordinated
     temporally by pulses of ecdysone. The biol. activity of this steroid
     hormone is mediated by two nuclear receptors: the ecdysone receptor (EcR)
     and the Ultraspiracle protein (USP). The crystal structure of the
     ligand-binding domain from the lepidopteran Heliothis virescens USP
     reported here shows that the loop connecting helixes H1 and H3 precludes
     the canonical agonist conformation. The key residues that stabilize this
     unique loop conformation are strictly conserved within the lepidopteran
     USP family. The presence of an unexpected bound ligand that drives an
     unusual antagonist conformation confirms the induced-fit mechanism
     accompanying the ligand binding. The ligand-binding pocket exhibits a
     retinoid X receptor-like anchoring part near a conserved arginine, which
     could interact with a USP ligand functional group. The structure of this
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RE.CNT 42

receptor provides the template for designing inhibitors, which could be

THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD

utilized as a novel type of environmentally safe insecticides.

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 25 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

```
Full
Text
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- AN 1998:116253 CAPLUS
- DN 128:151934
- TI Regulation of transcription by insect steroid hormones
- AU Fujiwara, Haruhiko; Matsuoka, Tomoko
- CS Grad. Sch. Sci., Univ. Tokyo, Tokyo, 113, Japan
- SO Kagaku to Seibutsu (1998), 36(2), 75-77 CODEN: KASEAA; ISSN: 0453-073X
- PB Gakkai Shuppan Senta
- DT Journal; General Review
- LA Japanese
- AB A review with 7 refs., on the mol. mechanism of metamorphosis regulation by ecdysone. The ecdysone-ecdysone receptor-ultraspiracle protein complex activates transcription of early genes and early-late genes. Transcription regulation mechanisms and functions of nuclear receptors (esp. DHR3) are discussed.
- L1 ANSWER 27 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

Full Text references

- AN 1997:805886 CAPLUS
- DN 128:44943
- TI Screening for ultraspiracle inhibitors as potential insecticides
- IN Heinrich, Julia N.; De La Cruz, Fernando; Kirsch, Donald R.
- PA American Cyanamid Company, USA
- SO PCT Int. Appl., 45 pp. CODEN: PIXXD2
- DT Patent
- LA English
- FAN.CNT 1

	PATENT NO.	KIND DATE	APPLICATION NO.	DATE
<u>PI</u>	WO 9745737	A1 19971204	WO 1997-US10212	19970530
	W: CA, JP			
	RW: AT, BE,	CH, DE, DK, ES, F	I, FR, GB, GR, IE, IT	, LU, MC, NL, PT, SE
	EP 912896	A1 19990506	EP 1997-928958	19970530
	R: AT, BE,	CH, DE, DK, ES, F	R, GB, GR, IT, LI, LU	, NL, SE, MC, PT,
	IE, FI			
	US 6110698	A 20000829	<u>US 1997-865960</u>	19970530
	JP 2000516085	T2 20001205	JP 1997-543090	19970530 ~
DDAT	TTG 100C 10017D	5 100005		

<u>PRAI</u> <u>US 1996–18817P</u> P 19960531 WO 1997–US10212 W 19970530

AB The invention relates to the identification of inhibitors of "orphan" nuclear receptors, or receptors for which no natural ligand is known. Specifically, it relates to the ultraspiracle protein, or Usp, of Drosophila melanogaster and homologues thereof in other insect species. A transformed yeast cell is provided, comprising an Usp binding partner, Usp or a deriv. thereof, an a reporter gene. Expression of the reporter gene requires the Usp-Usp binding partner complex. The transformed yeast is incubated in the presence and absence of the test compd. to form the test culture and control culture, resp., and expression of the reporter gene is monitored. The invention provides for identifying compds., variant nuclear proteins, and other auxiliary proteins that interfere with Usp function. Usp inhibitory compds. are useful as insecticides or as lead compds. for the development of insecticides.